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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,810	09/08/2003	Jean-Louis H. Dasseux	10173-104-999	1151

20583 7590 08/24/2004

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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,810	DASSEUX ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. The pending Application US 10/657,810 is a continuation of US 09,735,707, **now US Patent No. 6,680,203** (update is required). The application 09,735,707, now US Patent 6,680,203 is improperly named CIP of provisional application. "An application **claiming the benefits** of a provisional application under 35 U.S.C. 119(e) should not be called a "division" of the provisional application since the application will have its patent term calculated from its filing date, whereas an application filed under 35 U.S.C. 120, 121, or 365(c) will have its term calculated from the date on which the earliest application was filed, provided a specific reference is made to the earlier filed application(s), 35 U.S.C. 154(a)(2) and (a)(3)".

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,680,203. Although the conflicting claims are not identical, they are not patentably distinct from each other because the limitations of the independent claims 23 and 24 in the instant application absent from the parent case, i.e. "wherein the first peak profile and the second peak [**profile**] are obtained independently", or "not obtained concurrently" does not make it patentably distinct from the

parent case; two MS peak profiles should be obtained independently, since there is now way to run MS experiment to obtain two different peak profiles simultaneously. The limitation of claim 25 absent from the parent case, i.e. obtaining the first and the second peak profiles from the whole cell extracts, does not make it patentably distinct from the parent case, since the limitation of obtaining the first and the second peak profiles from the whole cell extracts was indicated in the Examiner's reasons for allowance for the parent case.

Claim Objections

4. Claims 23-25 are objected to because of the following informalities: in claim 23, step (b), third line, "at" is missing from "at least". The last sentence in claims 23-25 repeats step (c) and is unnecessary; besides it contains typos in "at least one molecules that differ[s]". Claim 58 refers to claim 5747. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear, what the expressions "wherein the first peak profile and the second peak profile are obtained independently" in claim 23 and "are not obtained concurrently" in claim 24 might mean, since it is not apparent, how the first and second peak profiles can be obtained "dependently", or "concurrently".

Claims 55 and 56 recite, "wherein the first FTMS peak profile is a historical control" and "concurrent control". What does it mean?

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. **Claim 23** is rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al. (US 6,329,146 B1) in view of Southern et al. (US 5,770,367).

Crooke discloses **mass spectrometric** methods, including FTMS, for biomolecular screening: "the present invention provides methods for the determination of the structure of biomolecular targets, as well as the site and nature of the interaction between ligands and biomolecular targets. The present invention also provides methods for the determination of the relative affinity of a ligand for the biomolecular target it interacts with. Also provided are methods for **screening ligand or combinatorial libraries of compounds against** one or **more**

than one biological target molecules. The methods of the invention also allow determination of the relative binding affinity of combinatorial and other compounds for a biomolecular target. The present invention further provides methods for the use of **mass modifying tags for screening multiple biomolecular targets**. In a preferred embodiment, ligands which have great specificity and affinity for molecular interaction sites on biomolecules, especially RNA can be identified. In preferred embodiments, such identification can be made simultaneously with libraries of ligands" (Abstract). "The binding agent may be a **"small" molecule**" (col. 5, lines 7-8). "**Comparison of ESI-MS_n mass spectra** generated, using this method, for RNA/DNA **in the presence and the absence of a binding ligand or drug** reveals the location of binding. This altered cleavage pattern is clearly discerned in the mass spectrum and correlated to the sequence and structure of the nucleic acid. Thus, the absolute binding affinity of the test ligand can be determined by the methods of the present invention. Comparison of the abundance of the nucleic acid-ligand noncovalent complex ion to the abundance of a similar complex ion generated from a standard compound (such as paromomycin for the 16S RNA A site) whose binding affinity is known, allows for the determination of relative binding affinity of the test ligand (col. col. 6, lines 27-40). The preparation step may include chromatography (col. 12, lines 53-67). "A further application of the present invention is the use **of mass spectrometric methods for the simultaneous screening of multiple biomolecular targets against combinatorial libraries or mixtures of compounds**. This rather complex screening procedure is made possible by the combined power of the mass spectrometric methods used and the way in which the screening is performed" (col. 7, lines 17-25).

"The methods of the present invention are applicable to the study of a wide variety of biomolecular targets that include, but are not limited to, **peptides, proteins**, receptors, antibodies, oligonucleotides, RNA, DNA, RNA/DNA hybrids, nucleic acids, modified oligonucleotides, peptide-nucleic acids (PNAs), oligosaccharides, carbohydrates, and glycopeptides. Further these biomolecular targets may be synthetic or isolated from natural sources. **Biomolecular targets of natural origin** include, but are not limited to, those obtained from microbial, plant, animal, viral or human materials, such as, but not limited to, **cells, cell extracts**, fluids, tissues and organs" (col. 29, lines 37-49).

Crooke does not specifically disclose mass spectrometric analysis of the cells.

Southern discloses mass spectrometric methods of screening e.g. nucleic acid probes encoded with mass spectrometry tags, applying plurality of reagents. Southern emphasizes: "many drugs are tissue-specific. Their action often depends on interaction with a cell-surface receptor. There are families of drugs based on core structures; for example, there are several comprising short peptides. It is useful to be able to trace candidate drugs to see which cells or tissues they may target. It would be useful to be able to trace many different candidates simultaneously. Using libraries of analytes tagged with coded mass-tags, it would be possible to trace interactions by examining cells or tissues in the mass spectrometer. If tags were attached by photolabile protecting groups, it would be possible to image whole animal or tissue sections using scanning laser cleavage, coupled with mass spectrometry" (col. 11, lines 51-64).

It would have been obvious to apply the method taught by Crooke directly to libraries of cells instead of biomolecular targets extracted from cells, because Southern emphasizes, that many drugs are tissue-specific, and therefore the comparative data obtained from FT-mass spectra of the cells treated and untreated by the drug candidates can give more precise information on the effect of the drugs candidate for the specific cells.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh
8/21/04